Claims

1. A method for identifying a compound that promotes the activity of osteoblasts, comprising:

(a) contacting at least one cell with a test compound *in vitro*;
(b) determining an activity of the Fhl2 gene or Fhl2 protein in the at least one cell;
(c) comparing the activity determined in (b) to the activity of the Fhl2 gene or Fhl2 protein in at least one control cell that has not been contacted with the test compound; and
(d) selecting the test compond if the activity measured in (b) is significantly different from that in the at least one control cell.

2. A method according to claim 1, comprising:

(a) contacting at least one cell with a test compound *in vitro*;
(b) measuring the level of *Fhl2* expression in the at least one cell;
(c) comparing the level of *Fhl2* expression measured in (b) to the level of *Fhl2* expression in at least one control cell that has not been contacted with the test compound; and
(d) selecting the compound if the level of *Fhl2* expression measured in (b) is higher than that in the at least one control cell.

3. A method according to claim 1, comprising:

(a) contacting at least one cell with a test compound *in vitro*;
(b) measuring the amount of Fhl2 protein in the nucleus of the at lest one cell;
(c) comparing the amount of Fhl2 protein measured in (b) to the amount of Fhl2 protein in the nucleus of the at least one control cell that has not been contacted with the test compound; and
(d) selecting the compound if the level of Fhl2 protein measured in (b) is higher than that in the control cell(s).

4. A method according to claim 1, comprising:

(a) contacting a test compound with at least one cell *in vitro*;

(b) determining the level of interaction between Fhl2 protein and Runx2 protein in the cell(s);

(c) comparing the level of interaction determined in (b) to the level of interaction between Fhl2 protein and Runx2 protein in at least one control cell that has not been contacted with the test compound; and

(d) selecting the compound if the level of interaction measured in (b) is significantly different from that in the control cell(s).

5. A method according to any one of claims 1 to 4 wherein the at least one cell is selected from the group consisting of primary osteoblasts, MC3T3-E1 cells, ROS17 cells and U2-OS cells.

6. A method for the preparation of a compound that is useful in the treatment of a bone disease, comprising:

(a) identifying a compound by a method according to any one of claims 1 to 5; and

(b) synthesizing the compound.

7. A compound that is useful in the treatment of a bone disease wherein the compound is capable of promoting osteoblast activity by enhancing the expression of the *Fhl2* gene, promoting the translocation of Fhl2 protein in the nucleus and/or modulating the interaction between Fhl2 protein and Runx2 protein.

8. A compound according to claim 7 wherein the compound is capable of enhancing signals mediated by Rho proteins.

9. The use of an *Fhl2* nucleic acid for the manufacture of a medicament for the treatment of a bone disease wherein the *Fhl2* nucleic acid is selected from the group consisting of

(a) polynucleotides comprising the sequence as shown in SEQ ID NO:1;

(b) polynucleotides comprising a sequence which has an identity of at least 50% to the sequence as shown in SEQ ID NO:1;

(c) polynucleotides hybridizing to the sequence as shown in SEQ ID NO:1 under stringent conditions;

(d) polynucleotides comprising a sequence which encodes a polypeptide having an amino acid sequence as shown in SEQ ID NO:2; and

(e) polynucleotides comprising a sequence which encodes a polypeptide having an amino acid sequence which has an identity of at least 70% to the amino acid sequence as shown in SEQ ID NO:2.

10. The use according to claim 9 wherein the *Fhl2* nucleic acid is a polynucleotide encoding a polypeptide having an amino acid sequence as shown in SEQ ID NO:2.

11. The use according to claim 9 or 10 wherein the *Fhl2* nucleic acid is a polynucleotide comprising the sequence as shown in SEQ ID NO:1.

12. The use according to any one of claims 9 to 11 wherein the bone disease is characterized by a decreased bone mass relative to that of non-diseased bone.

13. The use according to any one of claims 9 to 12 wherein the bone disease is osteoporosis.

14. The use according to any one of claims 9 to 13 wherein the *Fhl2* nucleic acid is overexpressed in osteoblasts.

15. A method of diagnosing a bone disease, comprising

(a) determining *in vitro* the level of expression of the *Fhl2* gene in tissue from an individual; and
(b) comparing the level determined in (a) to the level of expression of the *Fhl2* gene in control tissue;
so that if the level determined in (a) is lower than that of the control, the individual is diagnosed as exhibiting the bone disease.

16. A method according to claim 15 wherein the bone disease is osteoporosis.

17. The use of a transgenic non-human animal characterized by a decreased level of expression of the Fhl2 gene relative to that of the corresponding wild-type animal as an osteoporosis model.

18. The use according to claim 17 wherein the transgenic non-human animal is a knockout mouse.

19. A method for identifying a compound that promotes the activity of osteoblasts, comprising:

(a) administering a test compound to a transgenic non-human animal characterized by a decreased level of expression of the Fhl2 gene relative to that of the corresponding wild-type animal;

(b) determining an activity of the Fhl2 gene or Fhl2 protein;

(c) comparing the activity determined in (b) to the activity of the Fhl2 gene or Fhl2 protein in a control animal that has not been contacted with the test compound; and

(d) selecting the test compond if the activity measured in (b) is significantly different from that in the control animal.